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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,229	01/16/2002	Stephen Ginsberg	PENN-0797	6800

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EXAMINER
SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No.	Applicant(s)	
	10/050,229	GINSBERG ET AL.	
	Examiner	Art Unit	
	Jehanne Souaya Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1/2002
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1 and 3 are pending in the instant application. Claims 2 and 4 have been cancelled. An action on the merits of claims 1 and 3 follows.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite as it lacks a positive process step relating back to the preamble. The claim recites a method of identifying senile plaques, neurofibrillary tangles, and neuropil threads but the last positive step is detecting fluorescence in brain tissue. Therefore it is unclear if the claim is drawn to a method of identifying senile plaques, neurofibrillary tangles, and neuropil threads or to detecting fluorescence in brain tissue.

Claim 3 is indefinite as it lacks a positive process step relating back to the preamble. The preamble recites a method of diagnosing Alzheimer's disease but the last positive step is drawn to determining whether RNA hybridizes to known cDNAs. Accordingly, it is unclear if the method is a method of diagnosis or a method of hybridization.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Ginsberg et al (hereinafter referred to as Ginsberg, Ann Neurol, Feb. 1997, vol. 41, pages 200-209).

Ginsberg teaches a method of contacting senile plaques from postmortem brain tissue with acridine orange (see page 201, col 2) and determining fluorescence (see page 201-203, figure 1).

6. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Topaloglu et al (hereinafter referred to as Topaloglu; The anatomical record, vol. 224, pages 88-93, 1989).

The claims recite a method wherein brain tissue is contacted with a fluorescent dye capable of intercalating selectively into nucleic acids, and detecting any fluorescence in brain tissue. Topaloglu teaches contacting fetal rat brain tissue with acridine orange, which is a dye that intercalates into nucleic acids (see page 89, col. 1). Topaloglu teaches detecting fluorescence after acridine orange staining (see page 89, col. 2 and table 1).

7. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Mai et al (hereinafter referred to as Mai; The Journal of Histochemistry and Cytochemistry, vol 32, pages 97-104, 1984).

The claims recite a method wherein brain tissue is contacted with a fluorescent dye capable of intercalating selectively into nucleic acids, and detecting any fluorescence in brain tissue. Mai teaches contacting fetal rat brain tissue with acridine orange, which is a dye that intercalates into nucleic acids (see page 98, col. 1, "Staining"). Mai teaches detecting fluorescence after acridine orange staining (see page 99, col. 1 and figure 2).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ginsberg.

Ginsberg et al teach a method of contacting senile plaques from postmortem brain tissue with acridine orange (see page 201, col 2) and determining fluorescence (see page 201-203, figure 1). Ginsberg does not specifically teach having amplified the identified RNA or determining hybridization between the amplified RNA and cDNA for proteins involved in the pathogenesis of Alzheimer's disease, however, Ginsberg does teach to do so to characterize the identify of the RNA identified. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Ginsberg to add steps of amplifying the identified RNA and determining hybridization between the amplified RNA and cDNA for proteins involved in the pathogenesis of Alzheimer's disease because Ginsberg teaches to do so for the purpose of characterizing the transcripts.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,358,681.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '681 patent recite methods of identifying cytoplasmic RNAs in senile plaques, neurofibrillary tangles and neuropil threads comprising isolating senile plaques in brain tissue, contacting with a fluorescent dye capable of intercalating selectively into cytoplasmic RNAs present in the brain tissue, amplifying the identified RNA and determining whether the amplified RNA product hybridize to any known cDNAs for proteins involved in Alzheimer's disease. The instant claims are drawn to a method of contacting brain tissue with a fluorescent dye capable of intercalating selectively into nucleic acids and detecting fluorescence in the brain tissue. As such, the claims are coextensive in scope, with the claims of the '681 patent drawn to a species of the broader claim 1 recited in the instant application. The courts have stated that a genus is obvious in view of the teaching of a species. See Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). Therefore the instantly claimed method of identifying senile plaques, neurofibrillary tangles and neuropil threads is obvious in view of the method of detecting cytoplasmic RNA in senile plaques, neurofibrillary tangles and neuropil threads using the specific steps in claims 1 and 2 of the '681 patent.

13. Claim 3 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,358,681 in view of Johnson et al; (hereinafter referred to as Johnson, Science, vol. 248, pages 854-857, 1990).

The claims of the‘681 patent recite methods of identifying cytoplasmic RNAs in senile plaques, neurofibrillary tangles and neuropil threads comprising isolating senile plaques in brain tissue, contacting with a fluorescent dye capable of intercalating selectively into cytoplasmic RNAs present in the brain tissue, amplifying the identified RNA and determining whether the amplified RNA product hybridize to any known cDNAs for proteins involved in Alzheimer's disease. While the methods in the 681 patent are drawn to identifying RNA, and the claims of the instant application is drawn to diagnosing Alzheimer's disease, the method steps of the claims in the ‘681 patent are the same as those in the instant application. Additionally, Johnson teaches that an increase in APP-751/APP-695 mRNA provides a molecular marker for regional variations in senile plaque density in Alzheimer's disease patients (see abstract) and that APP-751/APP-695 mRNA ratio was twofold increased in senile plaques in AD versus non AD hippocampus. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of the claims in the 681 patent in a method of Alzheimer's disease diagnosis because claim 2 of the 681 patent recites a step of hybridizing the amplified RNA product to a known cDNA for a protein involved in the pathogenesis of Alzheimer's disease. Additionally, given the teachings of Johnson, it would have been prima facie obvious to the ordinary artisan that detection of mRNA encoding proteins involved in pathogenesis of Alzheimer's disease as in the method of either claim 1 or claim 2 of the ‘681 patent could be used in a method of diagnosing Alzheimer's disease. The ordinary artisan would have been motivated to use methods of claims of the ‘681 patent to diagnose Alzheimer's disease for the purpose of providing a reliable technique for diagnosing Alzheimer's disease.

Conclusion

14. No claims are allowable.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571) 272-0782. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Jehanne Sitton
Primary Examiner
Art Unit 1634

6/24/04